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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/052,121	01/17/2002	Cato T. Laurencin	DRE-0067	1682

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EXAMINER	
NAFF, DAVID M	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 11/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/052,121	LAURENCIN ET AL	
	Examiner	Art Unit	
	David M. Naff	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5 and 6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5 and 6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

An amendment of 9/19/05 amended 1.

Claims examined on the merits are 1-3, 5 and 6, which are all claims in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5 and 6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Support is not found in the specification for a pore size range of "from 500 to 860 μm" added by amendment in line 4 of claim 1. The specification (page 8, line 1) discloses microcarrier diameter as 500 to 860 μm, and not the pore size, which is disclosed as 113 to 356 μm (page 8, line 9).

In the amendment, applicants cite sections of the specification as providing support for the claim amendments. However, adequate support is not found in the sections cited for a pore size of from 500 to 860 μm.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are confusing and unclear by claim 1 reciting "interconnected" in both lines 5 and 6. Since line 6 requires an interconnected pore network, it is uncertain as to the purpose of reciting "interconnected" in line 5. Is this interconnected also a pore network, or is it something else that is interconnected.

Claim Rejections - 35 USC § 103

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Starling et al (6,210,715 B1) in view of Crotts et al for reasons in the previous office action of 6/17/05 and for reasons herein.

The claim is drawn to scaffold for tissue engineering comprising biodegradable polymer-based hollow microcarriers with a density equal to or less than water bonded together into an interconnected, three

dimensional scaffold having a pore size ranging from 500 to 860 μm that is a fully interconnected pore network.

Starling et al disclose microcarriers (also referred to as microspheres or microbeads) that can be used for cell culture (col 4, lines 32-35, col 5, lines 1-7 and col 6, lines 32-35),, or as an implant as a carrier of a pharmaceutical agent (col 9, lines 15 and 22, and col 9, line 57). The microspheres can be hollow, and be bonded together to form an aggregate of bonded together hollow microspheres (Figure 1-1 (1.4)). The hollow microspheres have a density of less than 1 gm/cc (col 6, line 54), and are bonded together by coating with calcium phosphate (CaP) and sintering to provide an aggregate having a density of about 1.00-1.12 gm/cc (col 6, line 60), preferably about 1.00-1.06 gms/cc (col 4, line 58). The hollow microspheres are made of a substrate, which can be calcium phosphate, glass, other oxide ceramics or polymers, proteinaceous materials or composite materials (col 5, line 66 to col 6, line 2). When the substrate material is polymeric or proteinaceous, bonding together of the hollow microspheres can involve heating the substrate material to soften the surface (col 6, lines 44-46). Polymeric/organic substrate materials for preparing the hollow microsphere include dextran, polyethylene, polypropylene, polystyrene, polyurethane and collagen (col 17, lines 36-39).

Crotts et al disclose preparing hollow microspheres composed of poly(D,L-lactic-co-glycolic acid) (PLGA) (page 91, abstract) that can be used as a carrier for drug delivery by encapsulating a drug (page

104, right col, lines 1-11). Poly(D,L-lactic acid) and its copolymers with glycolic acid are used as microsphere material due to their versatile biodegradability and biocompatibility (page 91, left col, under "Introduction"). The microspheres are prepared (page 93, left col, under "Microsphere preparation") by adding a water phase (with or without BSA (blood serum albumin)) to methylene chloride containing PLGA, generating an emulsion by ultrasonication, adding the emulsion to a PVA/PBS solution while being magnetically stirred, and continuing stirring for 2-3 h to permit evaporation of solvent. The microspheres are collected by centrifugation, washed and lyophilized, and size distribution is measured by using a series of stainless steel meshes.

It would have been obvious to use as the polymeric hollow microspheres of Starling et al, hollow microspheres made from PLGA as suggested by Crotts et al to obtain the property of PLGA having versatile biodegradability and biocompatibility as disclosed by Crotts et al. It would have been expected the PLGA hollow microspheres can be bonded together to form an aggregate of hollow microspheres by procedures disclosed by Starling et al. The aggregate when shaped as disclosed by Starling et al (col 9, lines 50-58) will be a scaffold as presently claimed. A pore size of 500 μm is suggested by Starling et al disclosing a pore size of 350-500 μm (col 9, lines 4-5).

Response to Arguments

Applicants urge that there must be motivation to combine the reference teaching. However, motivation has been set forth, i.e. to

obtain the property of PLGA having versatile biodegradability and biocompatibility.

Applicants urge that Crotts et al disclose microspheres ranging from 30-350 μm in size, whereas, the claims require a size of 500-860 μm. However, the claims require a pore size of 500-860 μm, and no size is specified for microcarrier size. In any event, Starling et al disclose a microsphere size of 500-1000 μm (col 9, line 1), and it would have been obvious to use sizes in this range when using microspheres made from PLGA as taught by Crotts et al. There is seen nothing to lead one to believe that microspheres cannot be made from PLGA having a size as taught by Starling et al. The references are combined together and must be considered together as a whole rather than each alone.

Applicants urge that pores of the claimed scaffold are interconnected. However, the aggregate of Starling et al has an interconnected porosity (col 6, line 32). When the particle size of the microspheres of Starling et al is within the range of 500-1000 μm, the pores will be fully interconnected.

Applicants urge that the scaffold of the invention has a density lighter than or as light as water. However, the claims do not use the term "light". In any event, density as light as water is a density equal to water as encompassed by the claims.

Claim Rejections - 35 USC § 103

Claims 2, 3, 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claim 1 above, and

further in view of Spaulding (6,001,643) and Granet et al (AJ on 1449) for reasons in the previous office action.

Claims 2 and 3 require the scaffold of claim 1 to be seeded with cells via culturing *in vitro* in a rotating bioreactor.

Claims 5 and 6 require a method of generating tissue by seeding the scaffold of claim 1 with cells that produce the tissue, and culturing the seeded cells in a rotating bioreactor.

Starling et al and Crotts et al are described above.

Spaulding discloses culturing cells in a roller bottle for implanting to produce tissue. Microcarrier beads having densities less than the cell culture medium can be used for cell attachment to constrain tissue constructs to the area surrounding the annular axis and away from the cylinder wall of the bottle (col 16, lines 25-30).

Granet et al disclose culturing osteoblastic cells on microcarriers in a rotating-wall vessel (page 514, section 2.1.2).

When preparing the aggregate of bonded together hollow microspheres of Starling et al using hollow microspheres made from PLGA as suggested by Crotts et al as set forth above, it would have been obvious to use the aggregate for cell culture as suggested by Starling et al, and carry out cell culture in a roller bottle as disclosed by Spaulding or in a rotating-wall vessel as disclosed by Spaulding since these culturing techniques are intended for culturing cells on a carrier. It would have been further obvious to provide the aggregate with a density less than that of water as suggested by Spaulding so the aggregate will surround the axis away from the wall.

Culturing cells such as osteoblast cells would have been obvious when the function of these cells is desired.

Response to Arguments

Applicants urge that Spaulding and Granet et al do not remedy the deficiencies in the teachings of Starling et al and Crotts et al. However, for reasons set forth above, Starling et al and Crotts et al are not believed deficient.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff

whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David M. Naff
Primary Examiner
Art Unit 1651

DMN
11/19/05